AMENDMENTS TO THE SPECIFICATION

Please amend the paragraph on page 2, lines 4-18, as follows:

Opportunistic infections to which individuals infected with HIV are susceptible include bacterial infections such as salmonellosis, syphilis and neurosyphilis, ~~turberculosis~~ tuberculosis (TB), atypical mycobacterial infection, and bacillary angiomatosis (cat scratch disease), fungal infections such as aspergillosis, candidiasis (thrush, yeast infection), coccidioidomycosis, cryptococcal meningitis, and histoplasmosis, protozoal infections such as cryptosporidiosis, isosporiasis, microsporidiosis, *Pneumocystis Carinii* pneumonia (PCP), and toxoplasmosis, viral infections such as *Cytomegalovirus* (CMV), hepatitis, herpes simplex (HSV, genital herpes), herpes zoster (HZV, shingles), human ~~papiloma~~ papilloma virus (HPV, genital warts, cervical cancer), *Molluscum Contagiosum*, oral hairy leukoplakia (OHL), and progressive multifocal leukoencephalopathy (PML), and neoplasms such as Kaposi's sarcoma, systemic non-Hodgkin's lymphoma (NHL), and primary CNS lymphoma, among others. These opportunistic infections remain principally responsible for the morbidity and mortality associated with HIV disease.

Please amend the paragraph on page 4, lines 2-11, as follows:

FIG. 1 is a set of graphs showing the response of primate peripheral blood mononuclear cells (PBMC) to K and D oligonucleotides (ODN). PBMC from 8-20 normal human donors and 20 rhesus macaques were stimulated for 72 hours with a panel of K, D or control ODN (3 mM). IL-6 and IFNα levels in culture supernatants were determined by ELISA while cell proliferation was assessed by $[H]^3$ thymidine uptake. Note that D ODN induce the secretion of IFNα while K ODN induce cell proliferation and IL-6 ~~producton~~ production. The response of PBMC from rhesus macaques mirrors that of human PBMC. All assays were performed in triplicate. Statistical significance was determined by ANOVA of log normalized data. A single asterisk (*) indicates a P value of <0.05; a double asterisk (**) indicates a P value of <0.01.

Please amend the paragraphs on page 5, line 26 to page 6, line 16, as follows:

FIG. 8 is a graph showing the effect of D and K ODN as adjuvants to the hepatitis B vaccine in rhesus macaques. Macaques (five/group) were immunized with ~~Engerix-B~~ hepatitis B vaccine ENGERIX-B™ (10 μg) alone or together with D or K ODN (250 μg/dose) on days 1, 30

and 60 of the study. Levels of IgG anti-hepatitis B surface antigen (HbsAg) were monitored by ELISA every two weeks. Macaques that received D or K ODN together with the vaccine developed significantly higher antibody levels compared to those that received the vaccine alone ($p<0.01$).

FIG. 9A-B is a pair of graphs showing that D and K ODN boost the immunogenicity of ~~Engerix-B~~ hepatitis B vaccine ENGERIX-B™ in SIV-infected rhesus macaques. SIV infected macaques were immunized on days 1, 30 and 75 with ~~Engerix-B~~ hepatitis B vaccine ENGERIX-B™ alone (n=5) or together with D or K ODN (n=6/group). Levels of IgG anti-HbsAg were monitored as described in Example 8. **FIG. 9A** is a graph showing the correlation of individual viral loads at the start of the study with the antibody titers developed 45 days after the prime and 45 days after the last immunization. One macaque from the group that received D ODN was euthanized during the study because of intractable diarrhea and weight loss attributed to the SIV infection. **FIG. 9B** is a graph showing the anti-HbsAg antibody levels by animals with viral loads $<10^7$ copies/ml (n=4/group). Animals that received the vaccine alone were unable to mount an antibody response, while those that received K or D ODN together with the HBV vaccine developed significant antibody levels.

Please amend the paragraph on page 7, lines 23-24, as follows:

CpG ODN: an ~~oligodexoynucleotide~~ oligodeoxynucleotide (either a D or a K type) including a CpG motif

Please amend the paragraph on page 8, line 6, as follows:

FDA: Food ~~ND drug~~ and Drug Administration

Please amend the paragraph on page 8, line 17, as follows:

HPV: human ~~papiloma~~ papilloma virus

Please amend the paragraph on page 9, line 27, as follows:

TB: ~~turberculosis~~tuberculosis

Please amend the paragraph on page 11, lines 20-24, as follows:

The known sequence of the CD4 precursor has a hydrophobic signal peptide, an ~~extracellular~~ extracellular region of approximately 370 amino acids, a highly hydrophobic stretch with significant identity to the membrane-spanning domain of the class II MHC beta chain, and a highly charged intracellular sequence of 40 resides (Maddon, *Cell* 42:93, 1985).

Please amend Table 1, beginning at page 13, line 6, as follows:

Table 1

Column A	Column B
indinavir ~~(Crixivan)~~ (CRIXIVAN™)	AZT/ddI
nelfinavir ~~(Viracept)~~ (VIRACEPT™)	d4T/ddI
ritonavir ~~(Norvir)~~ (VIRACEPT™)	AZT/ddC
saquinavir ~~(Fortovase)~~ (FORTOVASE™)	AZT/3TC
ritonavir/saquinavir	d4T/3TC

Please amend the paragraphs on page 14, line 22 to page 15, line 28, as follows:

Examples of infectious ~~virus~~ viruses include: *Retroviridae* (for example, human immunodeficiency viruses, such as HIV-1 (also referred to as HTLV-III, LAV or HTLV-III/LAV, or HIV-III) and other isolates, such as HIV-LP; *Picornaviridae* (for example, polio viruses, hepatitis A virus; enteroviruses, human coxsackie viruses, rhinoviruses, echoviruses); ~~*Calciviridae*~~ *Caliciviridae*(such as strains that cause gastroenteritis); *Togaviridae* (for example, equine encephalitis viruses, rubella viruses); *Flaviridae* (for example, dengue viruses, encephalitis viruses, yellow fever viruses); *Coronaviridae* (for example, coronaviruses); *Rhabdoviridae* (for example, vesicular stomatitis viruses, rabies viruses); *Filoviridae* (for example, ~~ebola~~ Ebola viruses); *Paramyxoviridae* (for example, parainfluenza viruses, mumps virus, measles virus, respiratory syncytial virus); *Orthomyxoviridae* (for example, influenza viruses); ~~*Bungaviridae*~~ *Bunyaviridae* (for example, Hantaan viruses, ~~bunga viruses~~ bunyaviruses, phleboviruses and Nairo viruses); ~~*Arena viridae*~~ *Arenaviridae* (hemorrhagic fever viruses); *Reoviridae* (for example, reoviruses, orbiviurses and rotaviruses); *Birnaviridae*; *Hepadnaviridae* (Hepatitis B virus); *Parvoviridae* (parvoviruses); *Papovaviridae* (papilloma viruses, polyoma viruses); *Adenoviridae* (most adenoviruses); *Herpesviridae* (herpes simplex virus (HSV)-1 and HSV-2, varicella zoster virus, cytomegalovirus (CMV), herpes viruses); *Poxviridae* (variola

viruses, vaccinia viruses, pox viruses); and *Iridoviridae* (such as African swine fever virus); and unclassified viruses (for example, the etiological agents of Spongiform encephalopathies, the agent of delta hepatitis (thought to be a defective satellite of hepatitis B virus), the agents of non-A, non-B hepatitis (class 1=internally transmitted; class 2=parenterally transmitted (for example, Hepatitis C); Norwalk and related viruses, and astroviruses).

Examples of infectious bacteria include: *Helicobacter ~~pyloris~~ pylori, Borelia burgdorferi, Legionella pneumophilia, Mycobacteria sps* (such as. *M. tuberculosis, M. avium, M. intracellulare, M. kansaii, M. gordonae*), *Staphylococcus aureus, Neisseria gonorrhoeae, Neisseria meningitidis, Listeria monocytogenes, Streptococcus pyogenes* (Group A *Streptococcus*), *Streptococcus agalactiae* (Group B *Streptococcus*), *Streptococcus* (*viridans* group), *Streptococcus faecalis, Streptococcus bovis, Streptococcus (anaerobic sps.), Streptococcus pneumoniae, pathogenic Campylobacter sp., Enterococcus sp., Haemophilus influenzae, Bacillus ~~anthracis~~ anthracis, corynebacterium diphtheriae, corynebacterium sp., Erysipelothrix rhusiopathiae, Clostridium perfringers, Clostridium tetani, Enterobacter aerogenes, Klebsiella pneumoniae, Pasturella multocida, Bacteroides sp., Fusobacterium nucleatum, Streptobacillus moniliformis, Treponema pallidium, Treponema pertenue, Leptospira,* and *Actinomyces israelli.*

Please amend the paragraphs on page 16, line 14 to page 17, line 2, as follows:

Lentivirus: A genus of the family ~~retroviridae~~ *Retroviridae* consisting of non-oncogenic retroviruses that produce multi-organ diseases characterized by long incubation periods and persistent infection. Lentiviruses are unique in that they contain open reading frames ~~(orfs)~~(ORFs) between the polymerase (pol) and envelope (env) genes and in the 3' env region. Five serogroups are recognized, reflecting the mammalian hosts with which they are associated. Lentiviruses include, but are not limited to human immunodeficiency virus, type 1 (HIV-1), human immunodeficiency virus, type 2 (HIV-2), simian immunodeficiency virus, agm (SIVagm), simian immunodeficiency virus, mnd (SIVmnd), simian immunodeficiency virus, syk (SIVsyk), simian immunodeficiency virus, col (SIVcol), Visna-Maedi virus (VMV), bovine immunodeficiency virus (BIV), feline immunodeficiency virus (FIV), caprine arthritis-encephalitis virus (CAEV), and equine infectious anemia virus (EIAV).

Leukocyte: Cells in the blood, also termed "white cells," that are involved in defending the body against infective organisms and foreign substances. Leukocytes are produced in the bone marrow. There are 5 main types of white blood cell, subdivided between 2 main groups: ~~polymorphonnuclear~~ polymorphonuclear leukocytes (neutrophils, eosinophils, basophils) and mononuclear leukocytes (monocytes and lymphocytes). When an infection is present, the production of leukocytes increases.

Please amend the paragraph on page 17, line 21 to page 18, line 2, as follows:

A "stabilized oligonucleotide" is an oligonucleotide that is relatively resistant to *in vivo* degradation (for example via an exo- or endo-nuclease). In one embodiment, a stabilized oligonucleotide has a modified phosphate backbone. One specific, non-limiting example of a stabilized oligonucleotide has a ~~phophorothioate~~ phosphorothioate modified phosphate backbone (wherein at least one of the phosphate oxygens is replaced by sulfur). Other stabilized oligonucleotides include: nonionic DNA analogs, such as alkyl- and aryl- ~~phophonates~~ phosphonates (in which the charged phosphonate oxygen is replaced by an alkyl or aryl group), and ~~phophodiester~~ phosphodiester and alkylphosphotriesters, in which the charged oxygen moiety is alkylated. Oligonucleotides that contain a diol, such as tetraethyleneglycol or hexaethyleneglycol, at either or both termini have also been shown to be substantially resistant to nuclease degradation.

Please amend the paragraph on page 18, line 19 to page 19, line 5, as follows:

Opportunistic infection: An infection that occurs in an immunocompromised subject. Opportunistic infections may result from treatments or from alterations in the immune system. The infectious agent can be viral, bacterial, protozoan, or fungal. Opportunistic infections can include, but are not limited to bacterial infections such as salmonellosis, syphilis and neurosyphilis, ~~turberculosis~~ tuberculosis (TB), atypical mycobacterial infection, and bacillary angiomatosis (cat scratch disease), fungal infections such as aspergillosis, candidiasis (thrush, yeast infection), coccidioidomycosis, cryptococcal meningitis, and histoplasmosis, protozoal infections such as cryptosporidiosis, isosporiasis, microsporidiosis, *Pneumocystis Carinii* pneumonia (PCP), and toxoplasmosis, viral infections such as *Cytomegalovirus* (CMV), hepatitis, herpes simplex (HSV, genital herpes), herpes zoster (HZV, shingles), human ~~papiloma~~

papilloma virus (HPV, genital warts, cervical cancer), *Molluscum Contagiosum*, oral hairy leukoplakia (OHL), and progressive multifocal leukoencephalopathy (PML), and neoplasms such as Kaposi's sarcoma, systemic non-Hodgkin's lymphoma (NHL), and primary CNS lymphoma, among others.

Please amend the paragraph on page 22, line 27 to page 23, line 15, as follows:

Certain K oligonucleotides are of the formula:

5' $N_1N_2N_3$T-CpG-W$N_4N_5N_6$ 3' (SEQ ID NO: 20)

and contain a phosphate backbone modification. In one specific, non-limiting example, the phosphate backbone modification is a phosphorothioate backbone modification (for example, one of the non-bridging oxygens is replaced with sulfur, as set forth in International Patent Application WO 95/26204, herein incorporated by reference). In one embodiment, K ODNs have a ~~phophorothioate~~ phosphorothioate backbone, and at least one unmethylated CpG dinucleotide. Eliminating the CpG dinucleotide motif from the K ODN significantly reduces immune activation. Incorporating multiple CpGs in a single K ODN increases immune stimulation. In some embodiments, the K ODNs are at least 12 bases long. In addition, K ODNs containing CpG motifs at the 5' end are the most stimulatory, although at least one base upstream of the CpG is required. More particularly, the most active K ODNs contain a thymidine immediately 5' from the CpG dinucleotide, and a TpT or a TpA in a position 3' from the CpG motif. Modifications which are greater than 2 base pairs from the CpG dinucleotide motif appear to have little effect on K ODN activity.

Please amend the paragraph on page 24, line 23 to page 25, line 11, as follows:

D CpG oligonucleotides can include modified nucleotides. Without being bound by theory, modified nucleotides can be included to increase the stability of a D oligonucleotide. Without being bound by theory, because phosphorothioate-modified nucleotides confer resistance to exonuclease digestion, the D ODN are "stabilized" by incorporating phosphorothioate-modified nucleotides. In one embodiment, the CpG dinucleotide motif and its immediate flanking regions include phosphodiester rather than phosphorothioate nucleotides. In

one specific non-limiting example, the sequence Pu_1 Py_2 CpG Pu_3 Py_4 includes phosphodiester bases. In another specific, non-limiting example, all of the bases in the sequence Pu_1 Py_2 CpG Pu_3 Py_4 are phosphodiester bases. In yet another specific, non-limiting example, $X_1X_2X_3$ and $X_4X_5X_6(W)_M(G)_N$ include phosphodiester bases. In yet another specific, non-limiting example, $X_1X_2X_3$ Pu_1 Py_2 CpG Pu_3 Py_4 $X_4X_5X_6(W)_M(G)_N$ include phosphodiester bases. In further non-limiting examples the sequence $X_1X_2X_3$ includes at most one or at most two ~~phosphothioate~~ phosphorothioate bases and/or the sequence $X_4X_5X_6$ includes at most one or at most two ~~phosphotioate~~ phosphorothioate bases. In additional non-limiting examples, $X_4X_5X_6(W)_M(G)_N$ includes at least 1, at least 2, at least 3, at least 4, or at least 5 ~~phosphothioate~~ phosphorothioate bases. Thus, a D oligodeoxynucleotide can be a phosphorothioate/phosphodiester chimera.

Please amend the paragraph on page 27, lines 4-10, as follows:

In one embodiment, the D oligodeoxynucleotides disclosed herein are at least about 16 nucleotides in length. In a second embodiment, a D oligodeoxynucleotide is at least about 18 nucleotides in length. In another embodiment, a D oligodeoxynucleotide is from about 16 nucleotides in length to about 100 nucleotides in length. In yet another embodiment, a D ~~oligodexoynucleotide~~ oligodeoxynucleotide is from about 16 nucleotides in length to about 50 nucleotides in length. In a further embodiment, a D oligodeoxynucleotide is from about 18 nucleotides in length to about 30 nucleotides in length.

Please amend the paragraph on page 27, lines 18-20, as follows:

The D oligodeoxynucleotide can include additional Gs at the 5'end of the oligodeoxynucleotide. In one specific example, about 1 or about 2 Gs are included at the 5' end of an ~~olgiodeoxynucleotide~~ oligodeoxynucleotide including a sequence as set forth as Formula IV.

Please amend the paragraph on page 28, lines 10-20, as follows:

The oligodeoxynucleotides disclosed herein can be synthesized *de novo* using any of a number of procedures well known in the art. For example, the oligodeoxynucleotides can be synthesized as set forth in U.S. Patent No. 6,194,388, which is herein incorporated by reference in its entirety. A D oligodeoxynucleotide may be synthesized using, for example, the B-cyanoethyl ~~phophoramidite~~ phosphoramidite method or nucleoside H-phosphonate method.

These chemistries can be performed by a variety of automated oligonucleotide synthesizers available in the market. Alternatively, oligodeoxynucleotides can be prepared from existing nucleic acid sequences (for example, genomic or cDNA) using known techniques, such as employing restriction enzymes, exonucleases or endonucleases, although this method is less efficient than direct synthesis.

Please amend the paragraph on page 29, line 7 to page 30, line 2, as follows:

Pharmaceutical compositions that include at least one immunostimulatory ODN as described herein as an active ingredient, or that include both an immunostimulatory ODN and an additional anti-viral, immunomodulatory, or anti-infective agent as active ingredients, may be formulated with an appropriate solid or liquid carrier, depending upon the particular mode of administration chosen. Additional active ingredients include, for example, antivirals such as AL-721 (from Ethigen of Los Angeles, CA), recombinant human interferon beta (from Triton Biosciences of Alameda, CA), Acemannan (from Carrington Labs of Irving, TX), ~~gangiclovir~~ganciclovir (from Syntex of Palo Alto, CA), didehydrodeoxythymidine or d4T (from Bristol-Myers-Squibb), EL10 (from Elan Corp. of Gainesville, GA), dideoxycytidine or ddC (from Hoffman-LaRoche), Novapren (from Novaferon Labs, Inc. of Akron, OH), zidovudine or AZT (from Burroughs Wellcome), ribavirin (from Viratek of Costa Mesa, CA), alpha interferon and acyclovir (from Burroughs Wellcome), Indinavir (from Merck & Co.), 3TC (from Glaxo Wellcome), Ritonavir (from Abbott), Saquinavir (from Hoffmann-LaRoche), and others, immuno-modulators such as AS-101 (Wyeth-Ayerst Labs.), bropirimine (Upjohn), gamma interferon (Genentech), GM-CSF (Genetics Institute), IL-2 (Cetus or Hoffman-LaRoche), human immune globulin (Cutter Biological), IMREG^{TM} (from Imreg of New Orleans, LA), SK&F106528, TNF (Genentech), and soluble TNF receptors (Immunex), anti-infectives such as clindamycin with primaquine (from Upjohn, for the treatment of pneumocystis pneumonia), fluconazlone (from Pfizer for the treatment of cryptococcal meningitis or candidiasis), nystatin, pentamidine, trimethaprim-sulfamethoxazole, and many others, and agents used in HAART therapy, such as nucleoside analog reverse transcriptase inhibitor drugs (NA), non-nucleoside analog reverse transcriptase inhibitor drugs (NNRTI), protease inhibitor drugs (PI).

Please amend the paragraphs on page 31, line 26, to page 32, line 15, as follows:

In some embodiments, the opportunistic infection is infection with Leishmania major. In other embodiments, the opportunistic infection is a bacterial infection such as salmonellosis, syphilis and neurosyphilis, ~~turberculosis~~ tuberculosis (TB), atypical mycobacterial infection, and bacillary angiomatosis (cat scratch disease), a fungal infection such as aspergillosis, candidiasis (thrush, yeast infection), coccidioidomycosis, cryptococcal meningitis, and histoplasmosis, protozoal infections such as cryptosporidiosis, isosporiasis, microsporidiosis, *Pneumocystis Carinii* pneumonia (PCP), and toxoplasmosis, or a viral infection such as *Cytomegalovirus* (CMV), hepatitis, herpes simplex (HSV, genital herpes), herpes zoster (HZV, shingles), human ~~papiloma~~ papilloma virus (HPV, genital warts, cervical cancer), *Molluscum Contagiosum*, oral hairy leukoplakia (OHL), and progressive multifocal leukoencephalopathy (PML), and neoplasms, such as Kaposi's sarcoma, systemic non-Hodgkin's lymphoma (NHL), and primary CNS lymphoma, among others.

In order to increase an immune response to an opportunistic infection in a subject infected with a lentivirus, a therapeutically effective amount of a D or K ODN (see above) is administered to the subject. In some embodiments, the ~~oligodexoynucleotide~~ oligodeoxynucleotide is a D oligodeoxynucleotide, and in some examples, the oligodeoxynucleotide is at least about 16 nucleotides in length and comprises a sequence represented by the following formula:

Please amend the paragraph on page 32, lines 24-29, as follows:

In some embodiments, $X_1X_2X_3$ and $X_4X_5X_6(W)_M(G)_N$ includes phosphodiester bases. In particular examples, $X_1X_2X_3$ includes one or more ~~phosphothioate~~ phosphorothioate bases, and in other examples, $X_4X_5X_6(W)_M(G)_N$ includes one or more ~~phosphothioate~~ phosphorothioate bases. In still other embodiments $X_1X_2X_3$ Pu Py and Pu Py $X_4X_5X_6$ are self complementary, and in further embodiments, the lentiviral infection is treated in subject without stimulating expression of CD4 in T cells of the subject.

Please amend the paragraph on page 34, lines 3-17, as follows:

Specific, non-limiting examples of antivirals include: AL-721 (from Ethigen of Los Angeles, CA), recombinant human interferon beta (from Triton Biosciences of Alameda, CA),

Acemannan (from Carrington Labs of Irving, TX), ~~gangiclovir~~ ganciclovir (from Syntex of Palo Alto, CA), didehydrodeoxythymidine or d4T (from Bristol-Myers-Squibb), EL10 (from Elan Corp. of Gainesville, GA), dideoxycytidine or ddC (from Hoffman-LaRoche), Novapren (from Novaferon Labs, Inc. of Akron, OH), zidovudine or AZT (from Burroughs Wellcome), ribavirin (from Viratek of Costa Mesa, CA), alpha interferon and acyclovir (from Burroughs Wellcome), Indinavir (from Merck & Co.), 3TC (from Glaxo Wellcome), Ritonavir (from Abbott), Saquinavir (from Hoffmann-LaRoche), and others.

Specific, non-limiting examples of immuno-modulators are AS-101 (Wyeth-Ayerst Labs.), bropirimine (Upjohn), gamma interferon (Genentech), GM-CSF (Genetics Institute), IL-2 (Cetus or Hoffman-LaRoche), human immune globulin (Cutter Biological), IMREG™ (from Imreg of New Orleans, LA), SK&F106528, TNF (Genentech), and soluble TNF receptors (Immunex).

Please amend Table 2, beginning at page 35, line 11, as follows:

Table 2

Column A	Column B
indinavir ~~(Crixivan)~~ (CRIXIVAN™)	AZT/ddI
nelfinavir ~~(Viracept)~~ (VIRACEPT™)	d4T/ddI
ritonavir ~~(Norvir)~~ (NORVIR™)	AZT/ddC
saquinavir ~~(Fortovase)~~ (FORTOVASE™)	AZT/3TC
ritonavir/saquinavir	d4T/3TC

Please amend the paragraph on page 36, lines 12-18, as follows:

Mononuclear cell preparation:

Human and monkey mononuclear cells were isolated by density gradient centrifugation of PBMC over ~~Ficoll-Hypaque~~ density gradient medium FICOLL™-Hypaque as described. Cells were washed three times and cultured in RPMI 1640 supplemented with 10% heat-inactivated fetal calf serum (FCS), 1.5 mM L-glutamine and 100 U/ml of penicillin/streptomycin at 5 x 10^5 cells/well in the presence of 1-3 μM ODN. Supernatants were collected after 72 hours and tested by ELISA for cytokine and antibody levels.

Please amend the paragraph on page 37, lines 11-28, as follows:

Experimental infections:

L. amazonensis (PH8) was obtained from American Type Culture Collection (~~Manasas~~Manassas, VA) and grown for infection. Promastigotes were grown in medium 199 with 20% FCS, supplemented by 0.1 mM adenine (Life Technologies, Gaithersburg, MD), 25 mM HEPES (Life Technologies), 5 µg/ml hemin (Sigma, St. Louis, MO), 1 µg/ml biotin (Life Technologies), and Pen/Strep/L-glutamine (Life Technologies). To ensure high infectivity, the strain was passed through BALB/c mice once and frozen as amastigotes for storage. These amastigotes were freshly transformed in culture to promastigotes, then grown to late log phase for each experiment. After washing the cells, metacyclic promastigotes were purified by negative selection using mAb D5, which recognizes a surface lipophosphoglycan determinant that is differentially expressed by procyclic and other immature stages of *L. amazonensis* promastigotes~~(E. Saraiva, unpublished)~~. The promastigotes were incubated for 30 minutes at room temperature with a 1/200 dilution of D5 ascites, and the agglutinated parasites were pelleted by low-speed centrifugation at 400 x *g* for five minutes. Metacyclic promastigotes remaining in suspension were pelleted and washed, then resuspended at 1 x 10^8 promastigotes/ml in RPMI. Monkeys were challenged by injection with 1 x 10^7 metacyclic promastigotes in 0.1 ml in the forehead.

Please amend the paragraphs on page 46, line 14 to page 47, line 19, as follows:

To compare the efficacy of D and K type ODN as adjuvants for the vaccine against hepatitis B, 15 two year-old rhesus macaques weighing 6 +/- 1 lbs. (five per group) were immunized with the pediatric dose of ~~Engerix-B~~ ENGERIX-B™ containing 10 µg of HBsAg adsorbed to alum alone or together with 250 µg of D or K type ODN. The animals were boosted 30 and 60 days later with the same product. All monkeys were negative for antibodies to HbsAg at baseline. Fourteen days after the first immunization, all macaques vaccinated with ~~Engerix-B~~ ENGERIX-B™ - D ODN had antibodies to HBV greater than 10mIU/ml, compared to only 60 and 80 % of those immunized with ~~Engerix-B~~ ENGERIX-B™ - K ODN or ~~Engerix-B~~ ENGERIX-B™ alone respectively. All animals developed protective levels (>10mIU/ml) of antibodies to HBV after the first boost. As shown in FIG. 8, animals that received K or D ODN as adjuvants developed significantly higher antibody levels (peak titer : 20469 +/- 2240 and

21702 +/- 1764 for K and D ODN respectively, compared to 9226 +/- 5237 for those animals that received the vaccine alone, p = 0.012). D and K type CpG ODN were equally effective as vaccine adjuvants for the hepatitis B vaccine.

Next, the efficacy of CpG ODN in eliciting a similar increase in antibodies to HbsAg in SIV infected rhesus macaques was assessed. Seventeen SIV infected animals were immunized with a pediatric dose of ~~Engerix-B~~ hepatitis B vaccine ENGERIX-B™ alone or together with 250 μg of D or K ODN. The animals were boosted 30 and 75 days after prime. The levels of IgG anti-HbsAg in sera were measured every two weeks for four months. Unlike healthy macaques, SIV infected animals were unable to mount a protective antibody response when immunized with the commercial hepatitis B vaccine alone, even after three immunizations. Only 20% of the animals immunized with ~~Engerix-B~~ ENGERIX-B™ alone had antibody levels greater than 10mIU/ml, and the mean peak level of antibodies produced was 9 +/- 7 mIU/ml. Among the animals that received the vaccine together with D or K ODN, the antibody titers achieved were inversely correlated with monkey's viral load at the start of the study (FIG. 9A). Indeed, animals with viral loads greater than $1x10^7$ copies/ml at the time of immunization were unable to mount a protective response to the vaccine regardless of the adjuvant used. Among those that had viral loads greater than 10^7 copies/ml, K and D ODN were similarly effective at promoting the development of anti-HbsAg antibodies (FIG. 9B). Although the antibody levels achieved were significantly increased relative to those macaques receiving the HBV vaccine alone, their absolute levels were significantly lower than those developed by healthy macaques ($p<0.001$).